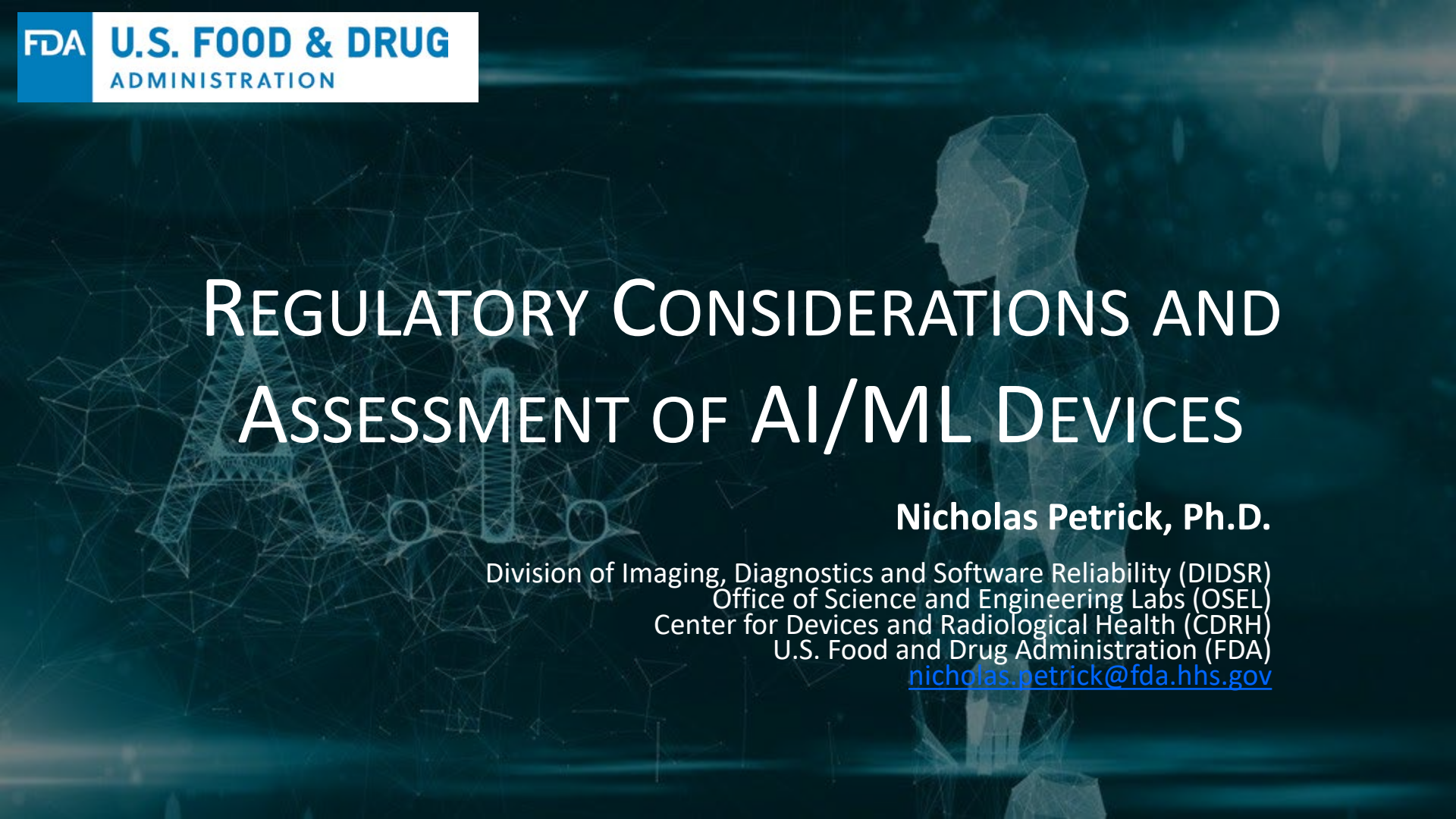


# Regulatory Considerations and Assessment of AI/ML Devices

**Nicholas Petrick, Ph.D.**

Division of Imaging, Diagnostics and Software Reliability (DIDSR)
Office of Science and Engineering Labs (OSEL)
Center for Devices and Radiological Health (CDRH)
U.S. Food and Drug Administration (FDA)
nicholas.petrick@fda.hhs.gov

# DISCLOSURES

- None

# OUTLINE

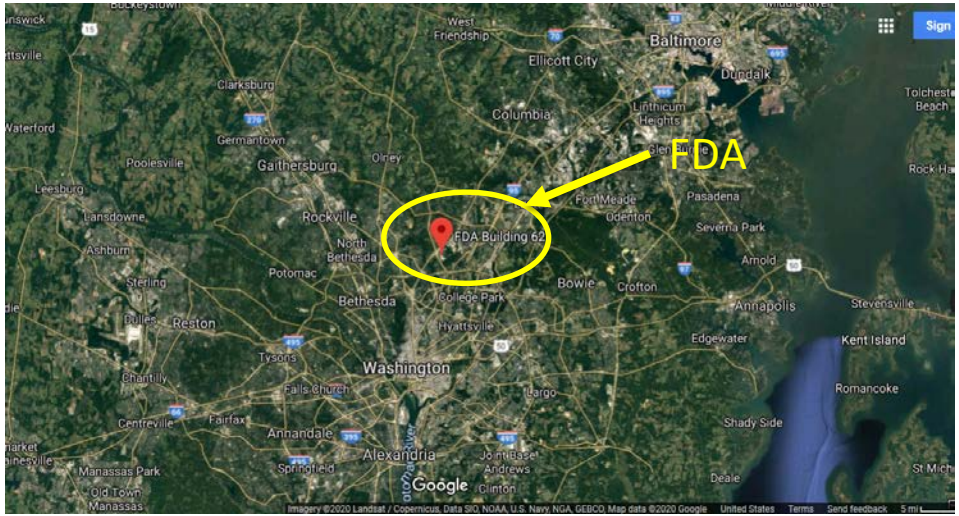
- What we do in CDRH/OSEL/DIDSR
- Device Regulations
- Software as a Medical Device (SaMD)
  - AI/ML development and assessment
- DIDSR AI/ML research areas

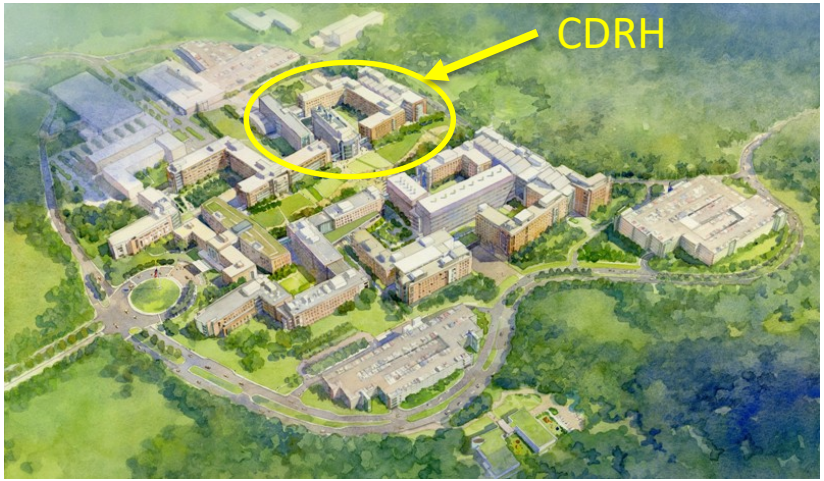
# INTRODUCTION

- Center for Device and Radiological Health
  - Office of Science And Engineering Labs
    - Division of Imaging, Diagnostics and Software Reliability

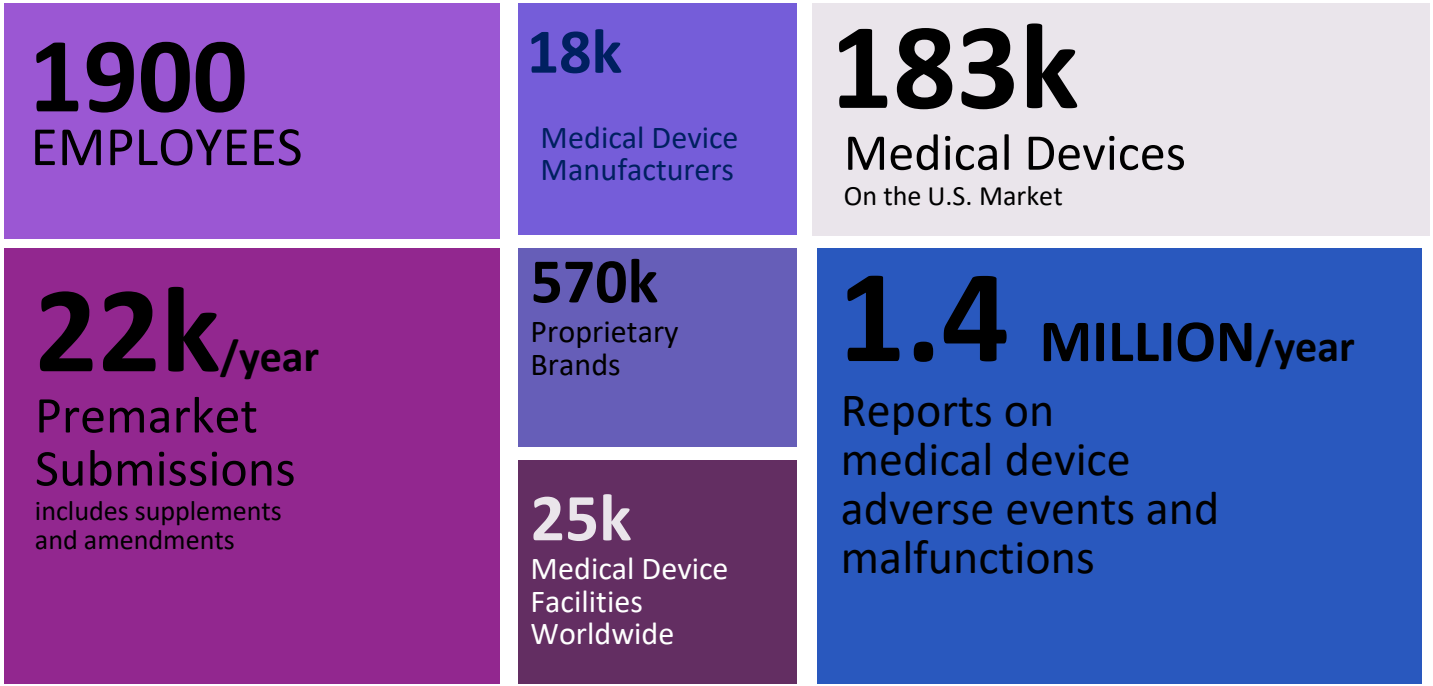
# FDA Campus

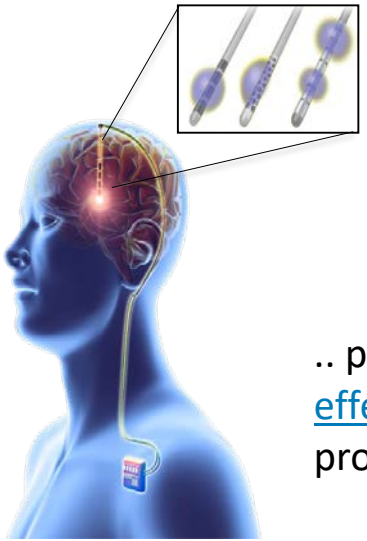
## Silver Spring, MD



# CDRH in Perspective

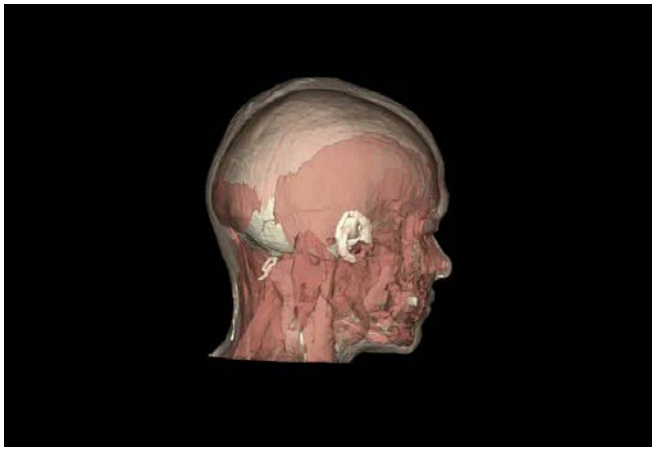




# CDRH Mission

.. protect and promote the health of the public by ensuring the safety and effectiveness of medical devices and the safety of radiation-emitting electronic products…

We facilitate medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and assuring consumer confidence in devices marketed in the U.S.



# OSEL

## Labs and Offices

# OSEL IN PERSPECTIVE

**183**
FEDERAL EMPLOYEES
Up to 180 visiting scientists

**140 Projects**
In 27 Laboratories and Program Areas

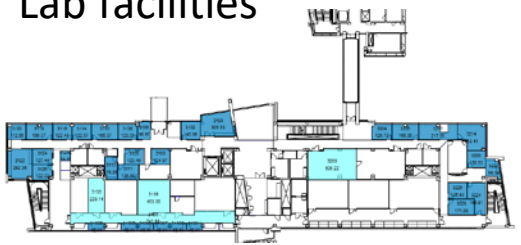
**400/year**
Peer reviewed presentations, articles, and other public disclosures

**2,500k/year**
Premarket Regulatory consults

**75**
Standards and conformity assessment committees

**70%**
Staff with post graduate degree

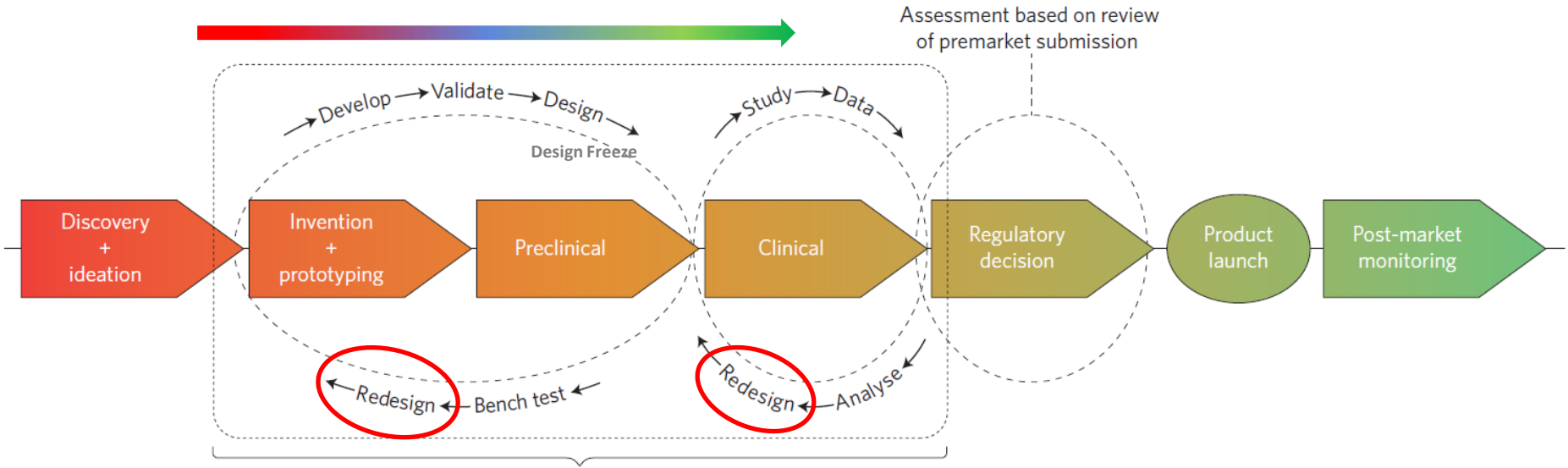
**55,000 ft²**
Lab facilities



# What OSEL Does

- Conduct laboratory-based regulatory research to facilitate development and innovation of safe and effective medical devices and radiation emitting products
- Provide scientific and engineering expertise, data, and analyses to support regulatory processes
- Collaborate with colleagues in academia, industry, government, and standards development organizations to develop, translate, and disseminate science and engineering-based information regarding regulated products

# WHY OSEL IS SO IMPORTANT



# DIDSR IN PERSPECTIVE

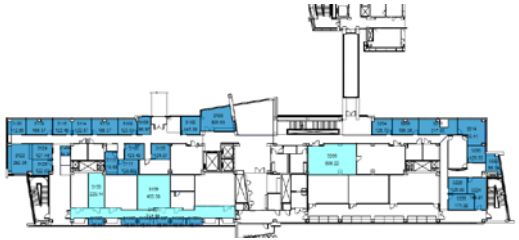
**35**
FEDERAL EMPLOYEES
14 Fellows/Students
3 Open Staff Positions

**145/year**
Peer reviewed articles, code and presentations

**5 Program Areas**
- AI/ML
- Credibility Assessment
- Digital Pathology
- Medical Imaging & Diagnostics
- Mixed Reality

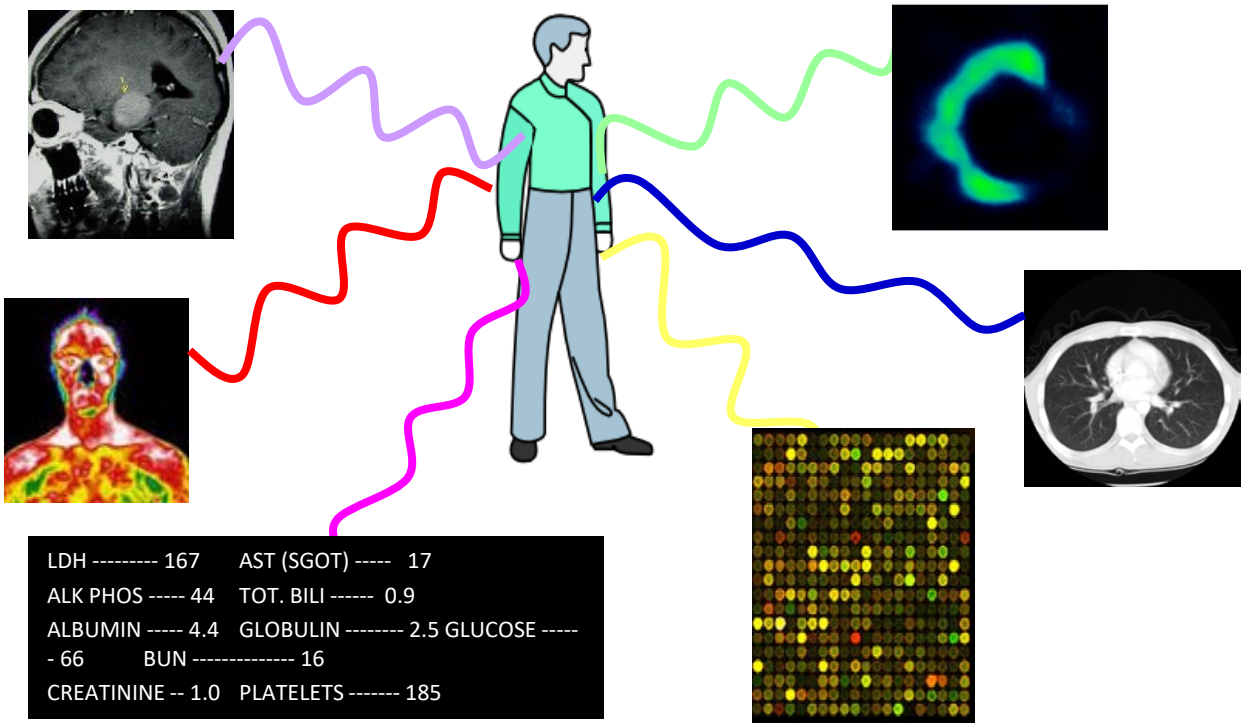
**550/year**
Premarket
Regulatory consults

**~15,000 ft²**
DIDSR Lab and facilities



# DIDSR

- Conducts laboratory research across a wide variety of imaging & diagnostic devices



# DIDSR'S OVERARCHING RESEARCH GOALS

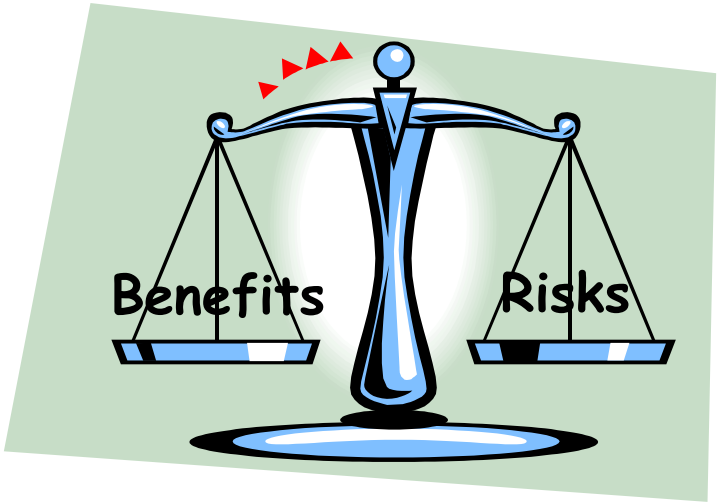
- Develop least burdensome approaches to clinical trials for imaging and big-data devices
  - Methods that account for reader variability, imperfect or missing reference standards, limited data for training and testing of machine classifiers, etc.

- Develop measures of technical effectiveness of imaging and big-data technologies as surrogates for clinical trials
  - Phantoms, lab measures, and computational models

# Device Regulations Overview

# CDRH Mission

- Protect and promote the health of the public by ensuring the safety and effectiveness of medical devices and the safety of radiation-emitting electronic products



# Device Class & Pre-Market Requirements

| Device Class | Controls | Premarket Review Process |
|---|---|---|
| Class I<br>(lowest risk) | General Controls | Most are exempt |
| Class II | General Controls<br>Special Controls | Premarket Notification [510(k)] |
| | | De Novo |
| Class III<br>(highest risk) | General Controls<br>Premarket Approval | Premarket Approval [PMA] |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# Device Class & Pre-Market Requirements

| Device Class | | Premarket Review Process |
|---|---|---|
| Class I<br>(lowest risk) | | Most are exempt |
| Class II | General Controls<br>Special Controls | Premarket Notification [510(k)] |
| | | De Novo |
| Class III<br>(highest risk) | General Controls<br>Premarket Approval | Premarket Approval [PMA] |

Demonstrate substantial equivalence to predicate device



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# Device Class & Pre-Market Requirements

| Device Class | | Premarket Review Process |
|---|---|---|
| Class I<br>(lowest risk) | | Most are exempt |
| Class II | General Controls<br>Special Controls | Premarket Notification [510(k)]<br>De Novo |
| Class III<br>(highest risk) | General Controls<br>Premarket Approval | Premarket Approval [PMA] |

Means for new device, without a valid predicate, to be classified into Class I or II



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# Device Class & Pre-Market Requirements

| Device Class | Controls | Premarket Review Process |
|---|---|---|
| Class I (lowest risk) | General Controls | Most are exempt |
| Class II | Special Controls | Premarket Notification [510(k)] |
| | | De Novo |
| Class III (highest risk) | General Controls<br>Premarket Approval | Premarket Approval [PMA] |

Demonstrate reasonable assurance of safety and effectiveness



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# Medical Devices By Class










**Class I**

**Class II**

CT, MR, US imaging systems
Any imaging AI/ML
Some IVD tests

**Class III**

Novel Imaging systems (DBT)
Leadless Pacemakers
Some AI/ML
Some IVD Tests

# Software as a Medical Device (SaMD)

IMDRF International Medical Device Regulators Forum

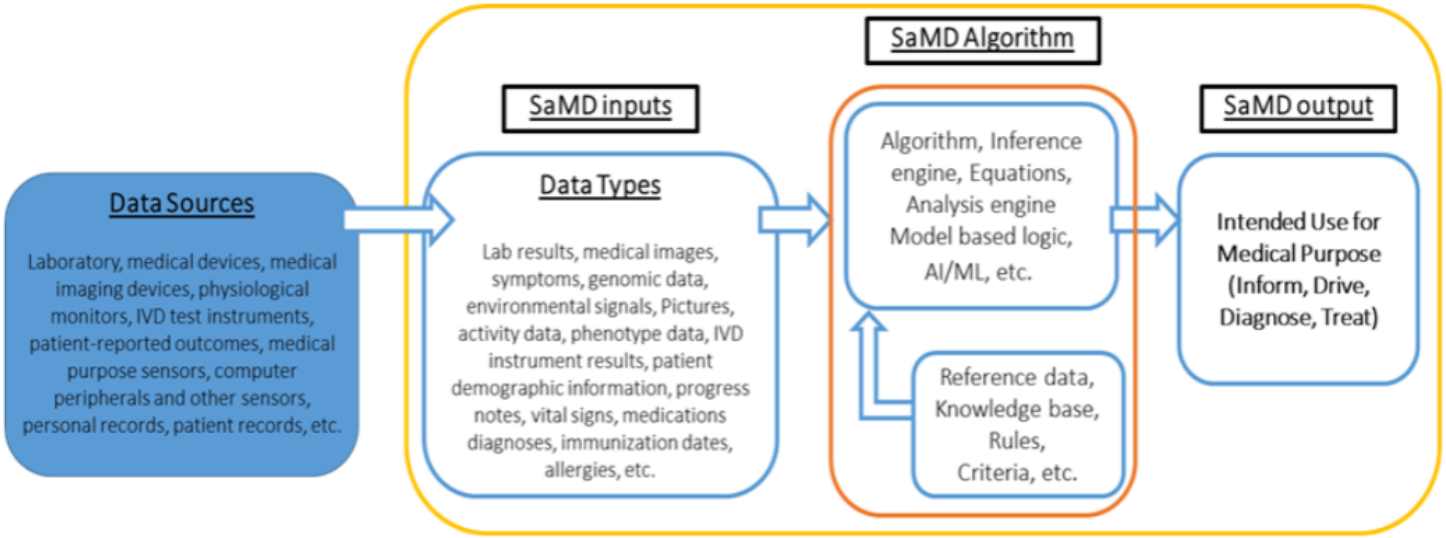
FDA

- IMDRF conceived 2011 as a forum to discuss future directions in medical device regulatory harmonization

- Voluntary group of medical device regulators from around the world … to accelerate international medical device regulatory harmonization and convergence

# SOFTWARE AS A MEDICAL DEVICE (SAMD)

*"Software as a Medical Device" (SaMD) is defined as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.*[5]



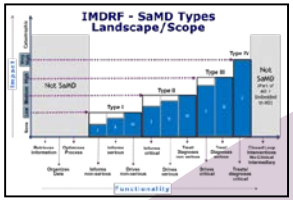

[5] http://www.imdrf.org/workitems/wi-samd.asp

# SaMD Examples

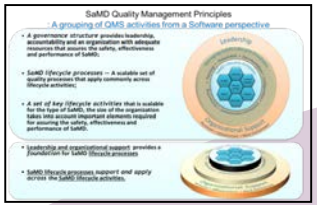
- Treatment planning software for radiation therapy
- Image display and processing software tools (PACS software)
- Software that detect lesions/conditions from diagnostic medical images
- Software that diagnoses lesions/conditions from diagnostic medical images
- Software making treatment recommendations from diagnostic images

# IMDRF Working Toward Global Convergence in Characterizing SaMD

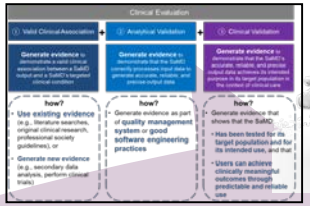

2013
Foundational vocabulary




2014 –
Risk framework based on impact to patients




2015 –
QMS control →Translating Software development practices to regulatory QMS



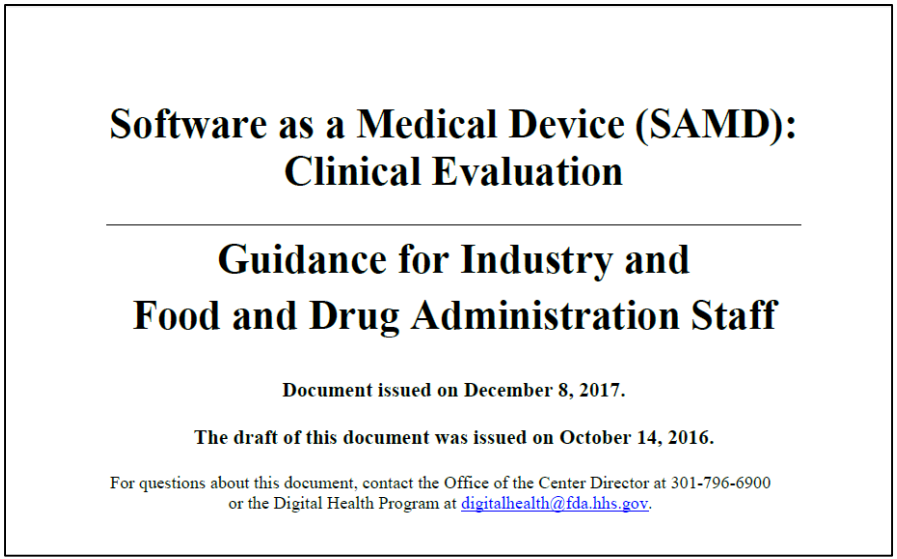


2017 – SaMD Clinical Evaluation → Generating evidence for clinically meaningful SaMD

IMDRF International Medical Device Regulators Forum

# IMDRF SAMD: Clinical Evaluation

- Adopted as FDA guidance in 2017
  - FDA adopted the converged principles of IMDRF in our evolving approach to SaMD review



**Software as a Medical Device (SAMD): Clinical Evaluation**

**Guidance for Industry and Food and Drug Administration Staff**

**Document issued on December 8, 2017.**

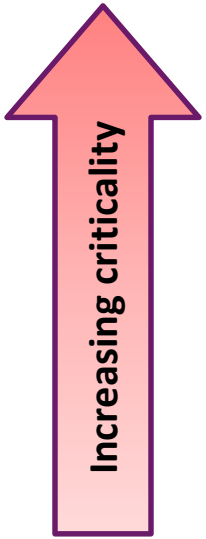
**The draft of this document was issued on October 14, 2016.**

For questions about this document, contact the Office of the Center Director at 301-796-6900 or the Digital Health Program at digitalhealth@fda.hhs.gov.

https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm524904.pdf

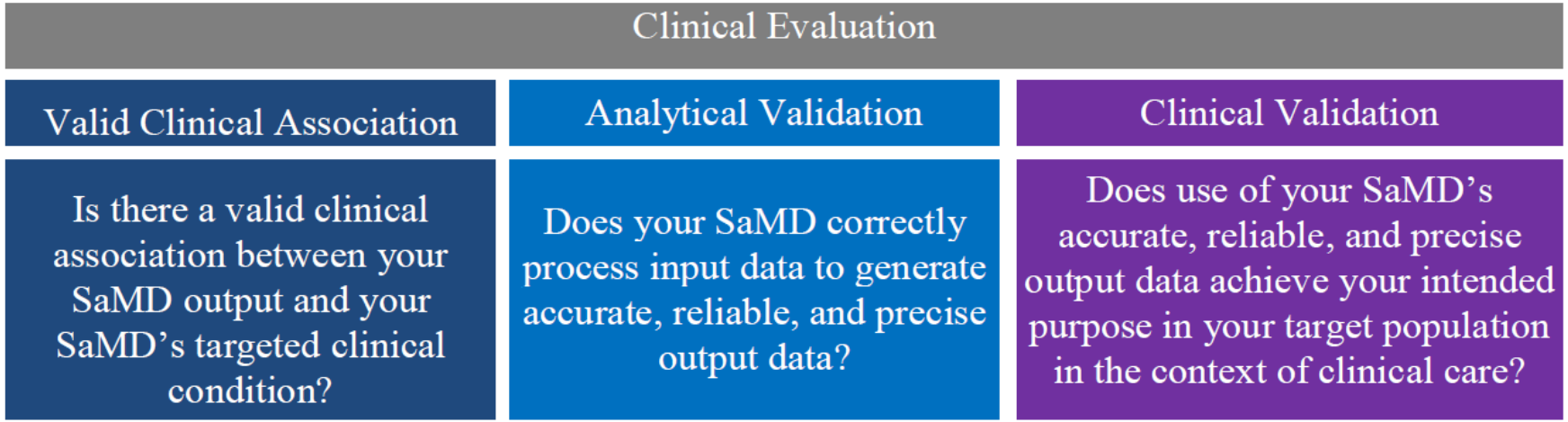
IMDRF International Medical Device Regulators Forum

# SaMD Risk Categories

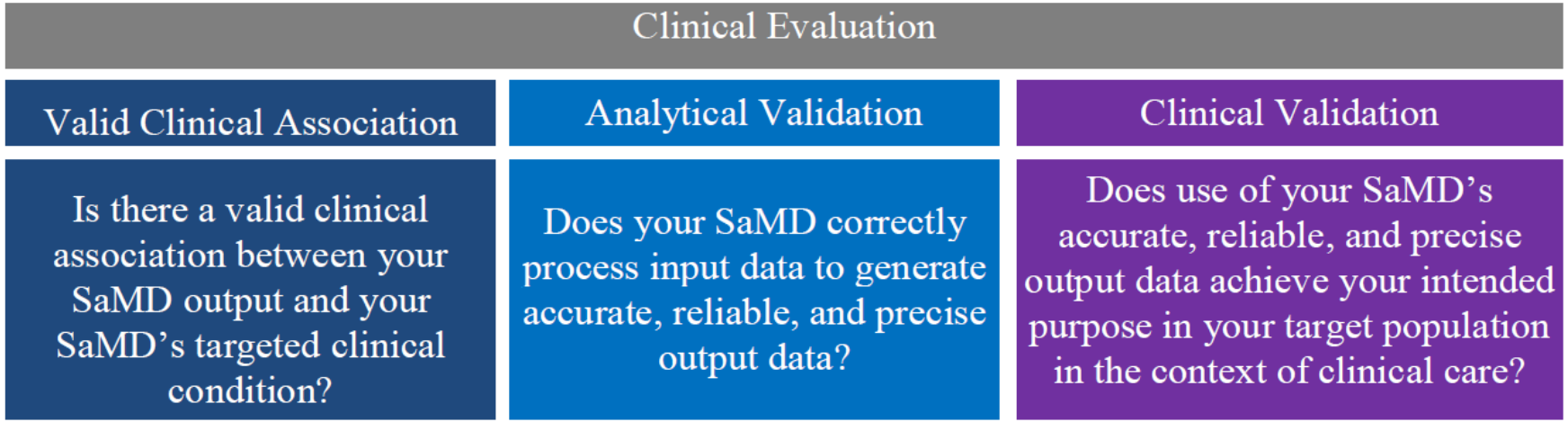

| State of Healthcare Situation or Condition | Significance of Information Provided by SaMD to Healthcare Decision | | |
|---|---|---|---|
| | Treat or Diagnose | Drive Clinical Management | Inform Clinical Management |
| Critical | IV | III | II |
| Serious | III | II | I |
| Non-Serious | II | I | I |

# SaMD: Clinical Evaluation



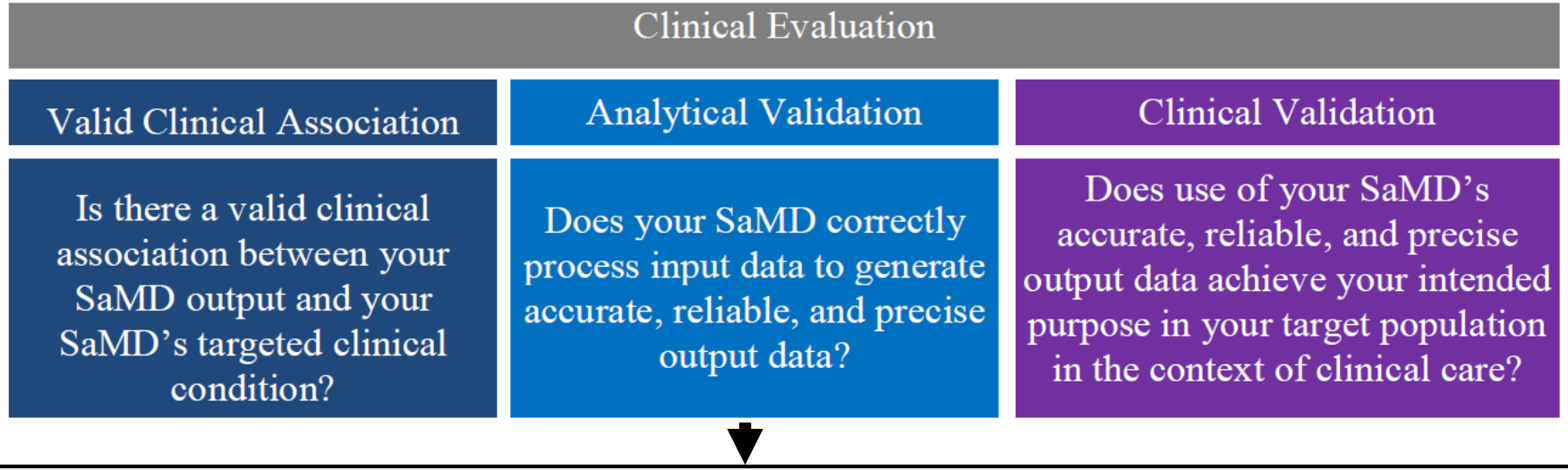

- Clinical association is indicator of level of clinical acceptance
  - How much meaning and confidence can be assigned to the clinical significance of the SaMD's output

# SaMD: Clinical Evaluation



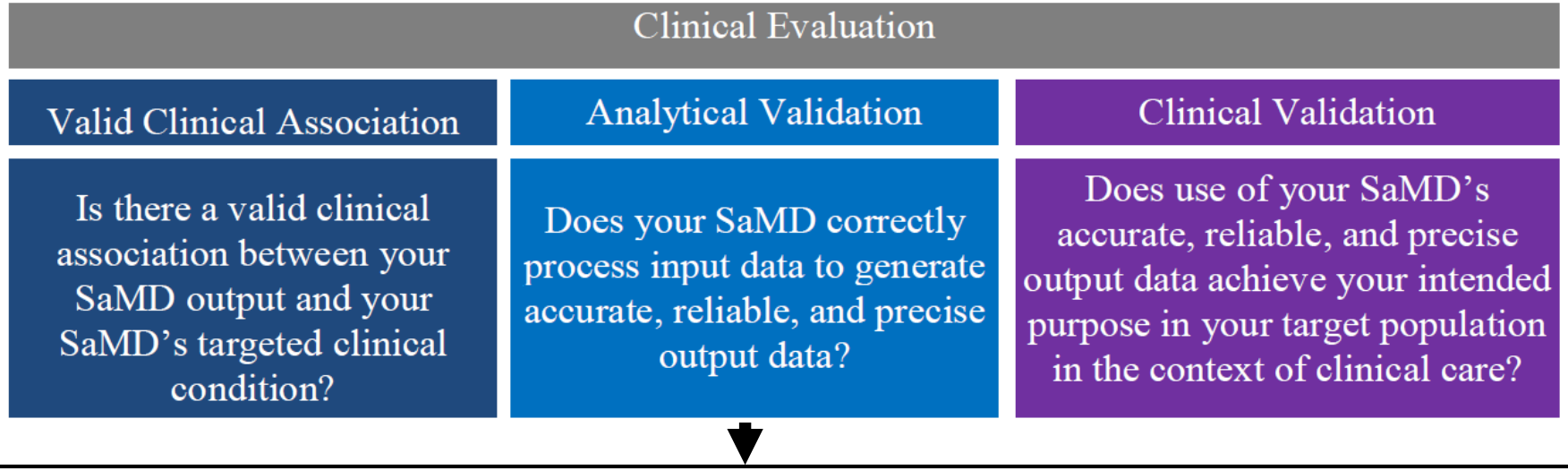

- Evidence generation
  - Literature
  - Professional guidelines
  - Secondary data analysis
  - Clinical trials/studies

# SaMD: Clinical Evaluation



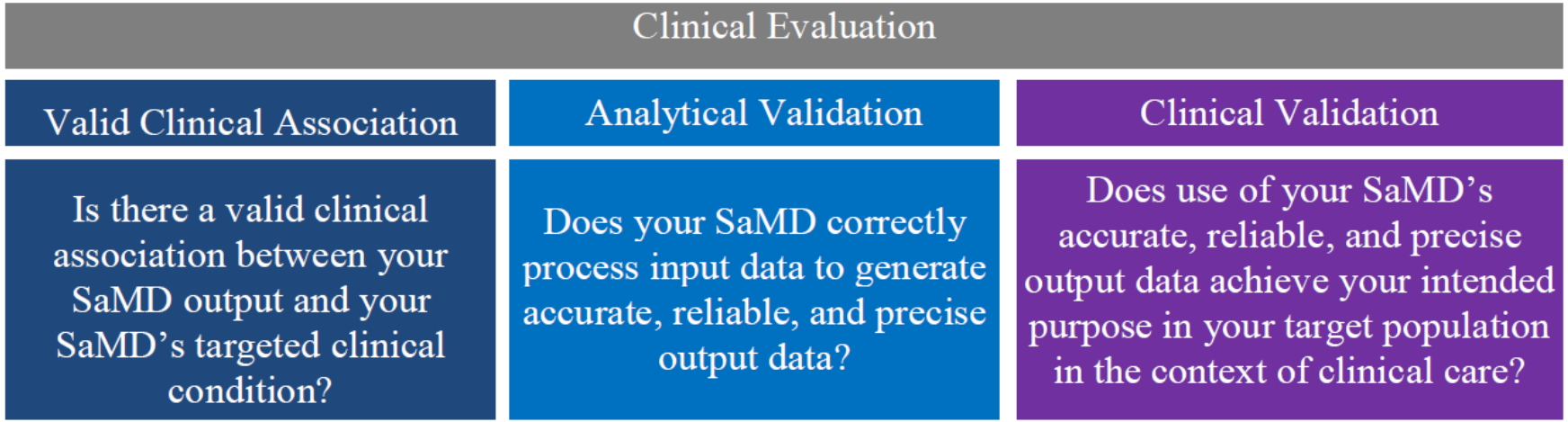

- Confirms and provides objective evidence SaMD meet technical requirements
  - Provide evidence that software correctly constructed
  - Demonstrate it meets specifications and conforms to user needs

# SaMD: Clinical Evaluation



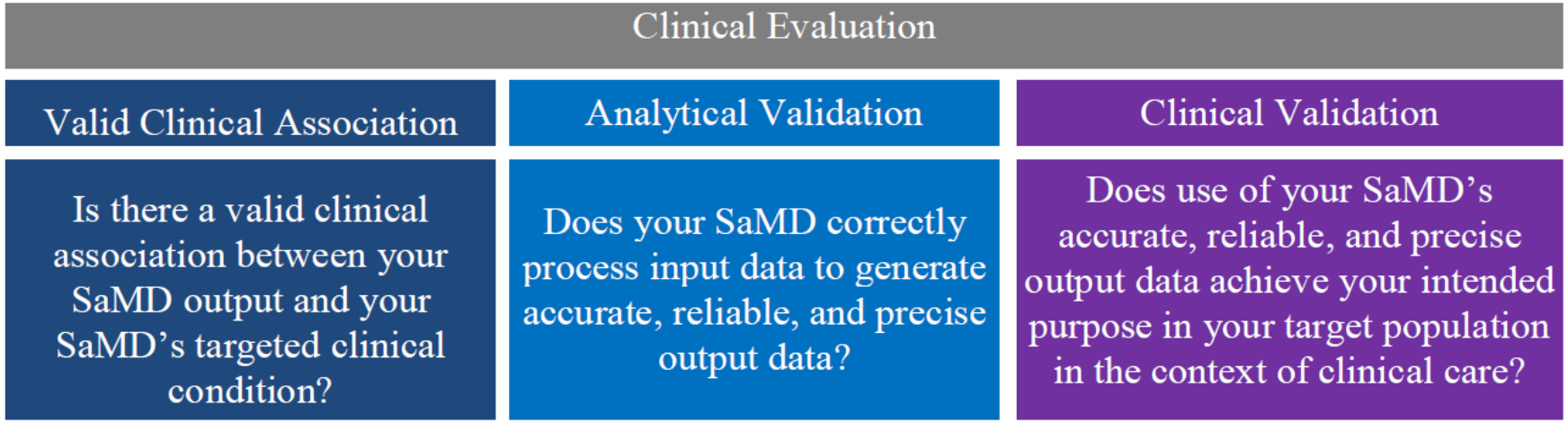

- Evidence generation
  - Verification and Validation (V & V) testing
    - Verification: objective evidence that specified requirements fulfilled
    - Validations: objective evidence that requirements for specific intended use or application fulfilled

# SaMD: Clinical Evaluation




- Clinical validation measures ability SaMD to yield clinically meaningful output associated
- Clinically meaningful means positive impact on the health of an individual or population

# SaMD: Clinical Evaluation



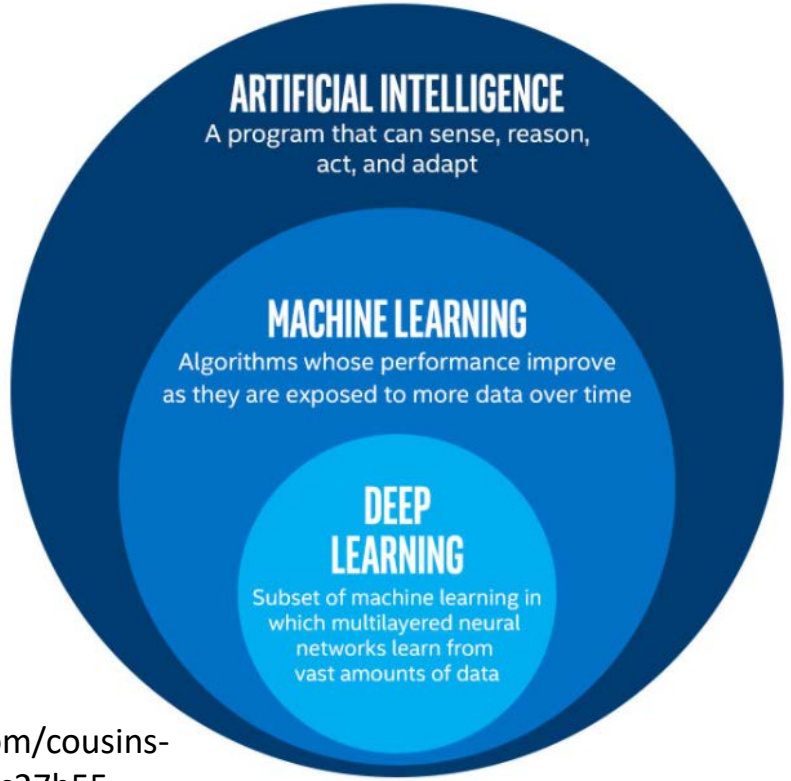

- Evidence generation
  - Existing data from studies for same intended use
  - Existing data from studies for a different intended use
    - Where extrapolation of such data can be justified
  - New clinical data for a specific intended use

# AI/ML SaMD

Assessment Framework

# INTRODUCTION

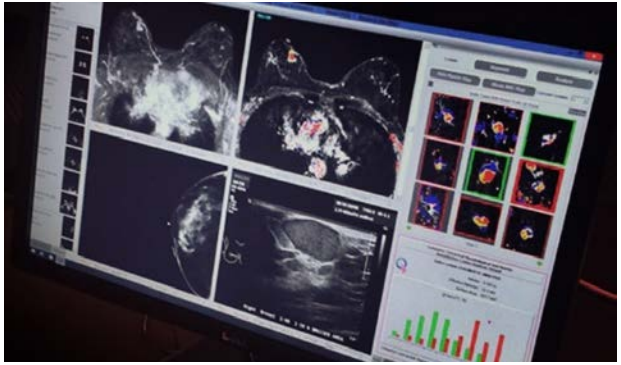
- AI
  - Algorithm that can sense, reason, act or adapt
- ML
  - Algorithms who's performance is based training with data
- Deep learning
  - ML based on multilayer neural network

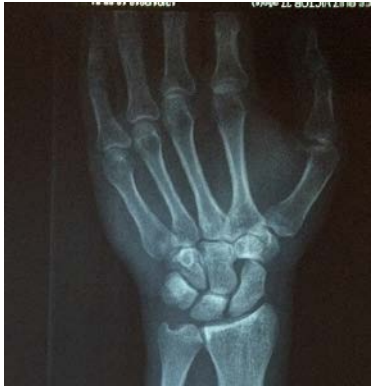



*https://towardsdatascience.com/cousins-of-artificial-intelligence-dda4edc27b55

# Many Devices Incorporating AI/ML in Medical Imaging

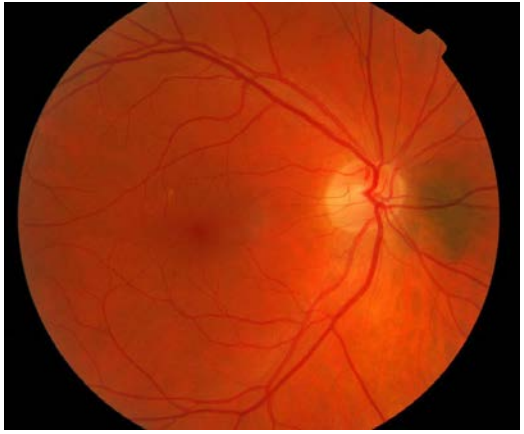
**Computer-Aided Classification of Breast Lesions on Magnetic Resonance Imaging:** Computer-Aided Diagnosis (CADx)





**Computer-Aided Detection and Diagnosis of Fractures on Radiographs:** CADe + CADx

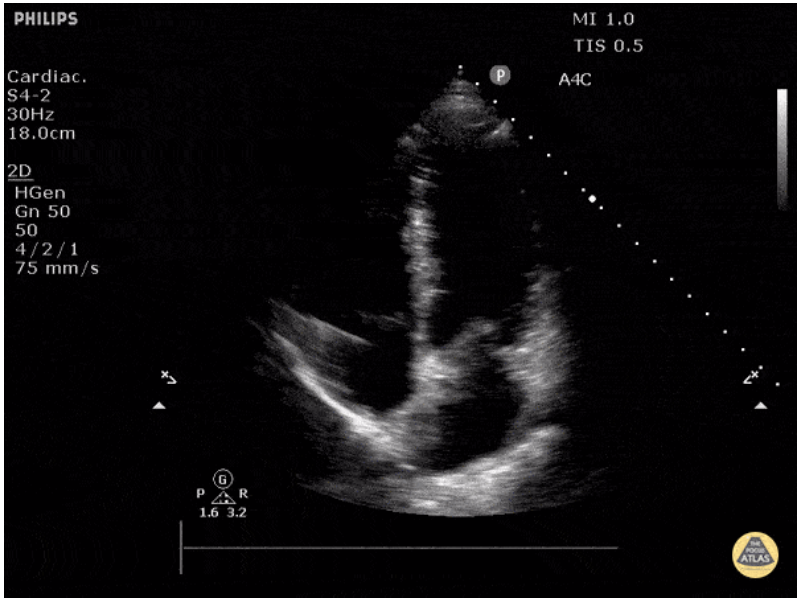
**Notification of Specialists for Suspicion of Stroke on Computerized Tomography Images:** Radiological Computer Aided Triage



**Detection of Diabetic Retinopathy on Retina Fundus Images:** Retinal Diagnostic Software

# AI/ML Interacting with HCPs

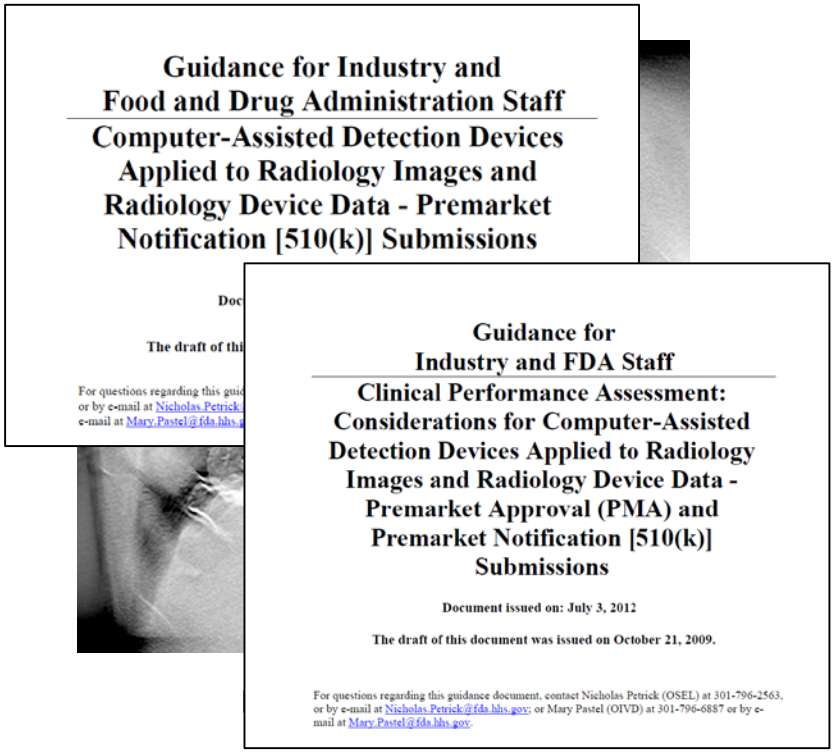
- Echocardiography
  - Cardiac sonography acquisition requires training and skill
  - AI can providing naïve users real-time guidance




http://www.thepocusatlas.com/echocardiography/sgz53ib6vai913wzgyn9qkhqo6ioe7

# ASSESSMENT OF IMAGING-BASED AI/ML

- Computer-aided Detection (CADe)
  - ML-based disease prompting devices
- FDA CADe Guidance documents




*Yamada et al, Radiol 287(1):333, 2018.

# Fundamentals of image-based ML SaMD Assessment

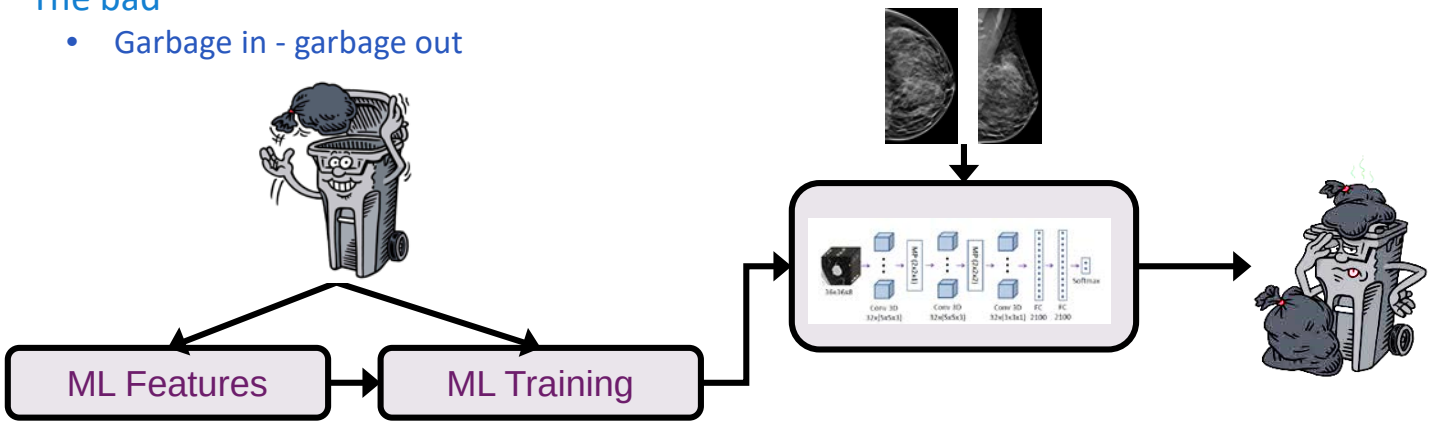
- Device description
- Data
- Performance assessment
  - Standalone performance
  - Reader performance (when appropriate)
  - …
- Human factors or other information/testing as appropriate
- …

# Device Description

- Device & algorithm descriptions
  - Device usage (mode of operation, patient population, …)
  - Algorithm design and function
    - Including structure of traditional and deep learning networks
    - Inputs
      - Type and range of signals/data
    - Outputs
  - Training process
  - Training/test database
  - Reference standard
  - …

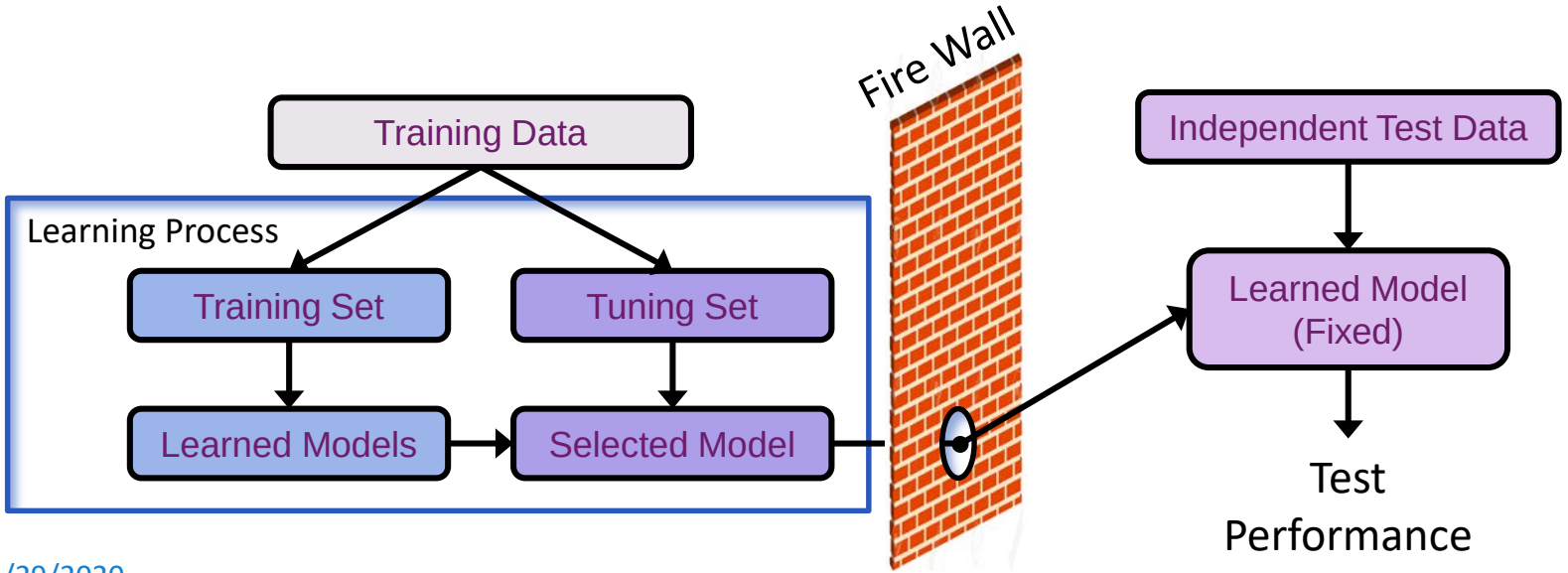
# DATA

- ML algorithms are data-driven
  - Versus, for example, physics or biology based
- ML algorithm development now facilitated by standardized ML platforms
  - Brings ML to a wider array of users
  - The good
    - Access to high-quality data streamlines design of novel ML applications
  - The bad
    - Garbage in - garbage out



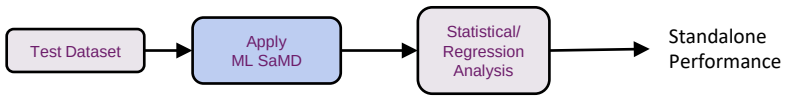
# PERFORMANCE TESTING

- Performance of ML algorithm on an independent data
  - Ideally, identifies problems with training process

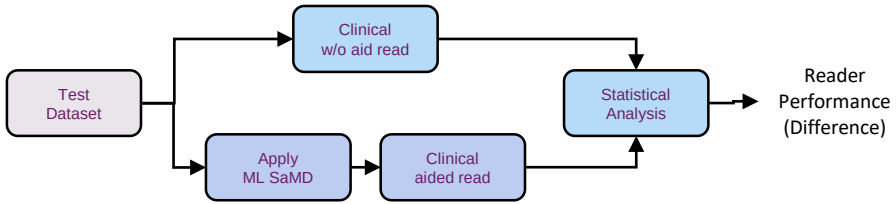


# PERFORMANCE TESTING

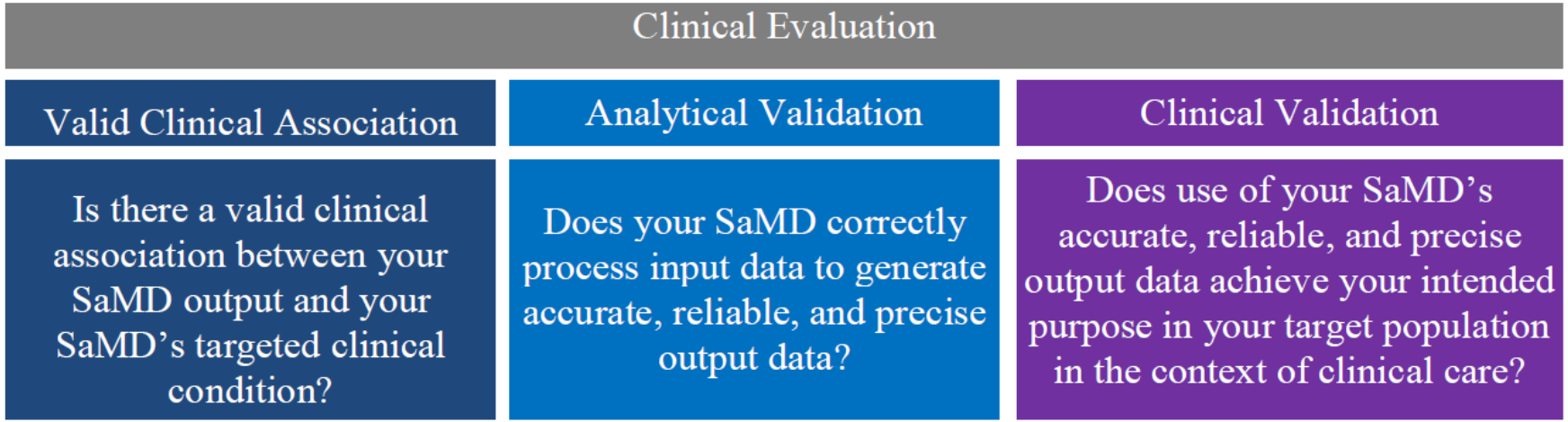
- Standalone performance
  - Performance of algorithm alone
  - Assesses robustness and generalizability of algorithm




- Clinical reader performance
  - Assessment of clinical aids
  - Clinicians' performance utilizing device
    - Multi-reader multi-case designs
    - Compare clinician's performance with the ML SaMD aid to without the aid

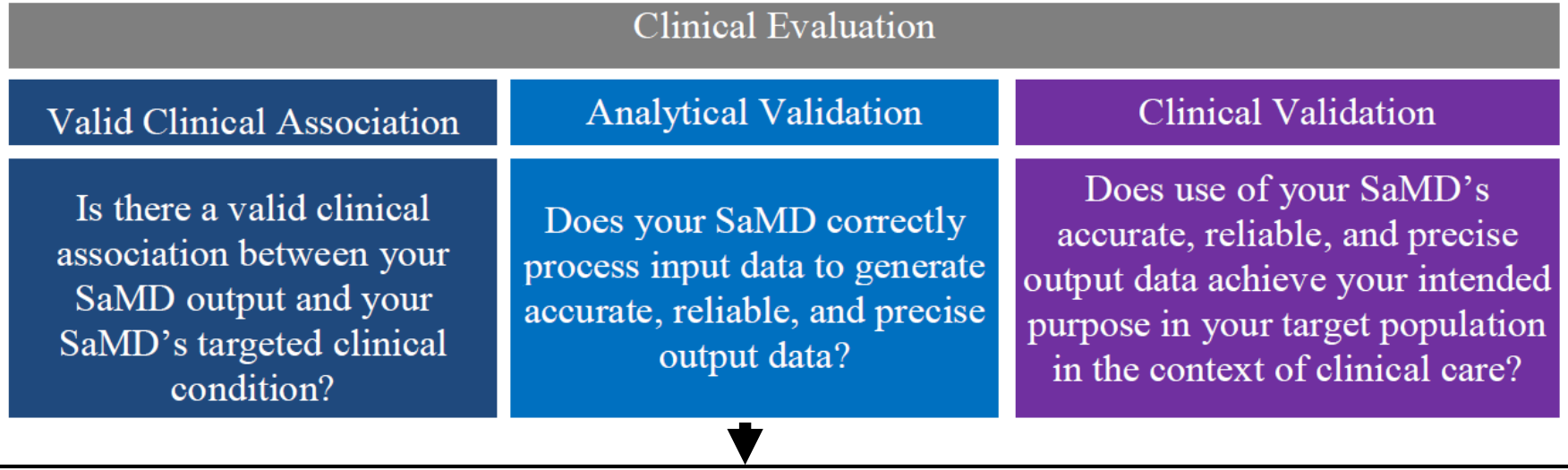


# CADe SaMD Evaluation



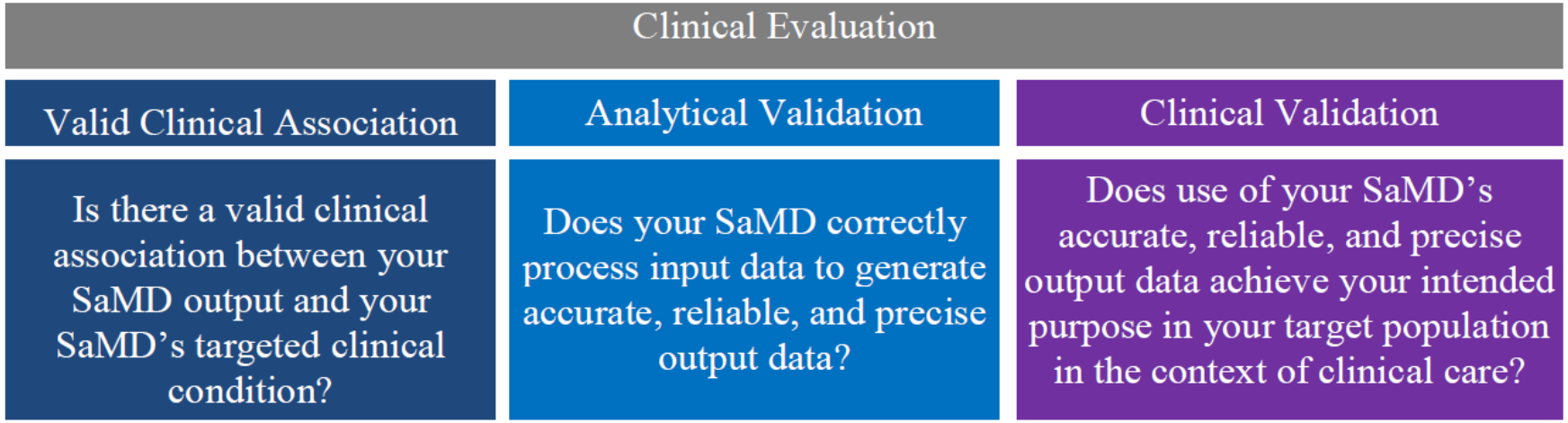

- Clinical Association
  - Likely from literature, professional guidelines
  - Device description used to support clinical association

# CADe SaMD Evaluation




- Analytical validation
  - Verification and validation testing of software
  - Standalone testing may support analytical validation, in part

# CADe SaMD Evaluation




- Clinical validation
  - Standalone performance
    - Establish performance of ML SaMD alone (compared to clinicians)
  - Clinical reader performance
    - Assess clinical aids provided by ML SaMD

# SUMMARY

- Who we are in CDRH
- Introduced to device regulation
  - Software as a Medical Device (SaMD)
  - Assessment framework imaging-based ML

# DIDSR INTERNSHIP AVAILABLE

- Postdoctoral fellowships and summer internships at all levels in OSEL/DIDSR
  - AI/ML
  - Color Quality
  - Computational modeling
  - Mixed Reality
  - Imaging system development
  - …

# ACKNOWLEDGMENTS


- I’ d like to acknowledge Berkman Sahiner for his help in developing this presentation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U.S. FOOD & DRUG
ADMINISTRATION